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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/899,575	07/05/2001	Jan Zur Megede	PP01631.102 (CHIR-1631/03	1709
Anne S. Dollar	7590 01 <i>/24/2</i> 00 d	7	EXAMINER	
CHIRON COR	PORATION	PARKIN, JEFFREY S		
Intellectual Property - R440 P.O. Box 8097			ART UNIT	PAPER NUMBER
Emeryville, CA	A 94662-8097		1648	
SHORTENED STATUTOR	Y PERIOD OF RESPONSE	MAIL DATE	DELIVER	Y MODE
3 MONTHS		01/24/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

1) ⊠ Responsive to communication(s) filed on 26 October 2006. 2a) ☐ This action is FINAL. 2b) ☑ This action is non-final. 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11, 453 O.G. 213. Disposition of Claims 4) ☑ Claim(s) 2-4,38 and 78-96 is/are pending in the application. 4a) Of the above claim(s) 2-4 and 78-96 is/are withdrawn from consideration. 5) ☐ Claim(s) is/are allowed. 6) ☐ Claim(s) 38 is/are objected to. 8) ☐ Claim(s) 38 is/are objected to. 8) ☐ Claim(s) are subject to restriction and/or election requirement. Application Papers 9) ☐ The drawing(s) filed on is/are: a) ☐ accepted or b) ☐ objected to by the Examiner. 10) ☐ The drawing(s) filed on is/are: a) ☐ accepted or b) ☐ objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a). Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d). The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152. Priority under 35 U.S.C. § 119 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) ☐ All b) ☐ Some * c) ☐ None of: 1. ☐ Certified copies of the priority documents have been received in Application No	•	Application No.	Applicant(s)				
Jeffrey S. Parkin, Ph.D. 1948		09/899,575	MEGEDE ET AL.				
- The MALING DATE of this communication appears on the cover sheet with the correspondence address — Period for Reply A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 03 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MALING DATE OF THIS COMMUNICATION. Extensions of them shy be available under the provisions of 37 CR1 1380, in one west, however, may a neigh be timely filled the communication of the provision of 37 CR1 1380, in one west, however, may a neigh be timely filled the provision of the communication. Feature to reply when the set or extended period for reply is patiently active the splication to beginnent. Set 37 CFR 17x(5) Any reply received by the Office later them entires after the mailing date of this communication, which is the provision of	Office Action Summary	Examiner	Art Unit				
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 02 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MALLING DATE OF THIS COMMUNICATION. and STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 02 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MALLING DATE OF THIS COMMUNICATION. and STATUTORY PERIOD FOR THE MALLING DATE OF THIS COMMUNICATION. IN Depend or reply is specified some, the maximum statutory period valing and valing loss (S) MONTHS from the mailing date of this communication. Finalize to reply whith the set or estimately period valing and valing loss (S) MONTHS from the mailing date of this communication. Finalize to reply whith the set or estimately period valing and valing loss (S) MONTHS from the mailing date of this communication, sever I finishly flex, may reduce any case replaced the mailing date of this communication, sever I finishly flex, may reduce any case replaced and the mailing date of this communication, sever I finishly flex, may reduce any case replaced and the mailing date of this communication, sever I finishly flex, may reduce any case replaced and the mailing date of this communication, sever I finishly flex, may reduce any case replaced and the mailing date of this communication. 1) Responsive to communication(s) filled on 26 October 2005. 2a) This action is splication is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Exparte Quayle, 1935 C.D. 11, 453 O.G. 213. Disposition of Claims 4) Claim(s) 2-4.38 and 78-96 is/are pending in the application. 4) Claim(s) 2-4.38 and 78-96 is/are withdrawn from consideration. 5) Claim(s) 2-4.38 and 78-96 is/are withdrawn from consideration. 5) Claim(s) 38 is/are objected to. 8) Claim(s) 38 is/are objected to. 8) Claim(s) 38 is/are objected to. 8) Claim(s) 38 is/are objected to. 9) The specification is objected to by the Examiner. 10) The drawing(s) filled on							
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Serial No.: 09/899,575 Docket No.: PP01631.102
Applicants: Zur Megede, J., et al. Filing Date: 07/05/01

Detailed Office Action

Status of the Claims

Claims 2-4, 38, and 78-96 are pending in the instant application. Claims 2-4 and 78-96 stand withdrawn from further consideration by the examiner, pursuant to 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention. Applicants again traverse the restriction requirement and submit that it would not constitute an undue burden if all sequences were searched concomitantly. The basis for the restriction requirement and the propriety of the requirement were adequately address in the last office action mailed 04 April, 2006.

37 C.F.R. § 1.98

Applicants are reminded that the information disclosure statement filed 30 June, 2005, was placed in the application file and the information referred to therein was considered. However, as previously set forth, applicants are reminded that the information disclosure statement filed 09 June, 2003, failed to comply with the provisions of 37 C.F.R. § 1.97, 1.98 and M.P.E.P. § The IDS listed 64 patent documents, 128 foreign patent documents, and 154 non-patent literature documents. Because the excessive number of references would constitute an undue burden on the examiner, they have not been considered since a statement identifying their relevance to the claimed invention has not been provided. Accordingly, the IDS was placed in the application file, but the information referred to therein was not considered as to the merits. Applicants noted that these references were previously supplied in U.S. Serial No. 09/610,313. However, perusal of this application failed to identify the various documents cited or a description identifying their relevance.

Serial No.: 09/899,575
Applicants: Zur Megede, J., et al.

37 C.F.R. § 1.821-1.825

application contains sequence disclosures that This encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Applicants are reminded that sequences Sequence Disclosures. appearing in the specification (e.g., see page 107) and/or drawings (e.g., see Figure 105) must be identified by a sequence identifier (SEQ ID NO.:) in accordance with 37 C.F.R. § 1.821(d). identifiers for sequences appearing in the drawings may appear in the Brief Description of the Drawings. Applicant must provide appropriate amendments to the specification and/or drawings inserting the required sequence identifiers. Extensive amendments may necessitate the submission of a substitute specification.

Claim Objections

Claim 38 is objected to because of the following informalities: the claim references non-elected nucleotide sequences. Applicants are reminded of the original restriction requirement set forth in the office action mailed 05 January, 2005, and the petition decided and mailed 28 January, 2006. The claim language should be amended to reflect the election. Appropriate correction is required.

37 C.F.R. § 1.57(d)

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (e.g., see pages 36 and 50). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See

Serial No.: 09/899,575 Applicants: Zur Megede, J., et al.

M.P.E.P. § 608.01.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The previous rejection of claim 38 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is hereby withdrawn in response to applicants' arguments.

Allowable Subject Matter

SEQ ID NO.: 120 appears to be free of the prior art and would be allowable with appropriate claim amendments (i.e., An expression cassette comprising a polynucleotide encoding a modified immunogenic human immunodeficiency virus type 1 (HIV-1) Env glycoprotein wherein said polynucleotide comprises SEQ ID NO.: 120). Applicants are invited to contact the examiner to discuss suggested revisions to the claim language.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may

Serial No.: 09/899,575 Applicants: Zur Megede, J., et al.

be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.

Primary Examiner

21 January, 2007

Notice to Comply

Application No. Applicant(s) 09/899.575 Zur Megede, J., et al. Examiner Art Unit Jeffrey S. Parkin

Paper No. 1648 01/27/2007

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

\boxtimes	1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
	2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
	3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
	4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
	5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
	6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
ide sec app	7. Other: applicants are reminded that Sequences appearing in the specification and/or drawings must be ntified by a sequence identifier (SEQ ID NO.:) in accordance with 37 C.F.R. § 1.821(d). Sequence identifiers for puences appearing in the drawings may appear in the Brief Description of the Drawings. Applicant must provide propriate amendments to the specification and/or drawings inserting the required sequence identifiers. Extensive endments may necessitate the submission of a substitute specification.

Applicant May Need to Provide:

- An substitute computer readable form (CRF) copy of the "Sequence Listing".
- An substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

- For Rules Interpretation, call (571) 272-0951
- For Patentin Software Program Help, call Patent EBC at 1-866-217-9197 between the hours of 6 a.m. and 12 midnight, Monday through Friday, EST.
- Send e-mail correspondence for Patentin Software Program Help @ ebc@uspto.gov.

To Download Patentin Software, visit http://www.uspto.gov/web/patents/software.htm.

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY

Synthetic HIV Type C expression cassettes provides dramatic increases in production of their protein products, relative to the native (wild-type Subtype C) sequences, when expressed in a variety of cell lines.

5 B. Signal Peptide Leader Sequences

The ability of various leader sequences to drive expression was tested by transfecting cells with wild type or synthetic Env-encoding expression cassettes operably linked to different leader sequences and evaluating expression of Env polypeptide by ELISA or Western Blot. The amino acid and nucleotide sequence of various signal peptide leader sequences are shown in Table 4.

Table 4

Leader	Amino acid sequence	DNA sequence	
WTnative (8_2_TV 1_C.ZA)	MRVMGTQKNCQQWWIWGI LGFWMLMIC	ATGAGAGTGATGGGGACACAGA AGAATTGTCAACAATGGTGGATA TGGGGCATCTTAGGCTTCTGGAT GCTAATGATTTGT	
WTmod (8_2_TV 1_C.ZA)	MRVMGTQKNCQQWWIWGI LGFWMLMIC	ATGCGCGTGATGGGCACCCAGAA GAACTGCCAGCAGTGGTGGATCT GGGGCATCCTGGGCTTCTGGATG CTGATGATCTGC	
Tpal	MDAMKRGLCCVLLLCGAVFVSPS AS	ATGGATGCAATGAAGAGAGGGC TCTGCTGTGTGCTGCTGTGTG GAGCAGTCTTCGTTTCGCCCAGC GCCAGC	
Tpa2	MDAMKRGLCCVLLLCGAVFVSPS	ATGGATGCAATGAAGAGAGGGC TCTGCTGTGTGCTGCTGTGTG GAGCAGTCTTCGTTTCGCCCAGC	

293 cells were transiently transfected using standard methods with native and sequence-modified constructs encoding the gp120 and gp140 forms of the

8_2_TV1_C.ZA (TV1c8.2) envelope. Env protein was measure in cell lysates and supernatants using an in-house Env capture ELISA. Results are shown in Table 5 below and indicate that the wild-type signal peptide leader sequence of the TV1c8.2 can be used

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\downarrow : is the regions for β -sheet deletions

*: is the N-linked glycosylation sites for subtype C TV1 and TV2. Possible mutation $(N \rightarrow Q)$ or deletions can be performed.

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(1) ----MDAMKRGLCCŸLLŢCĠAVFŶSPSAVĒKŢŴŸŢŸŢŶŢŶŢŶWĶEATŦŢŢ
        SF162
                       (1) MRVMGTQKNCQQWWIWGILGFWMLMICNTEDLWWRLYYGVPWWRDAXTTL
    TV1.8 2
                       (1) MRVMGTQKNCQQWWIWGILGFWMLMICNTEDIWFTYWGJPWWREAKTTL
(1) MRARGILKNYRHWWIWGILGFWMLMMCNYKGLMYTWYGJFWGREAKTTL
    TV1.8 5
TV2.12-5/1
                             MRVMGTQKNCQQWWIWGILGFWMLMICNVEDLWVTVYYGVPVWREAKTŢL
 Consensus
                      (47) FCASDAKAYDTEVHNIWATHACIPPTEPNEDEIVLENYTENENMIKNINGE
(51) FCASDAKAYETEVHNIWATHACIPTEDINDOBIVICANYTENENMIKNINAD
(51) FCASDAKAYETEVHNIWATHACIPTEPPNEDEIVLENTIMIKNIMAD
(51) FCASDAKAYEKEVHNIWATHACIPTOPNEDEVALCHITENFUMIKNIMAD
        SF162
     TV1.8_2
     TV1.8_5
TV2.12-5/1
                       (51) PCASDAKAYETEVHNVWATHACVPTDPNPQEIVLGNVTENFNMWKNNMVD
  Consensus
                                                                       β2/V1V2/β3
                                                                                                           * 150
                              OMHEDIĪSLŅDOSLKEÇĪVETĒLÇVELHCĪNLKNATNTK----SSN---
OMHEDIĪSLŅDOSLKESĪKUS DEĞTĪLVCĪDTNVTGNRTVTGNRTNUTNG
OMHEDIĪSLŅDOSLKESĪKUS DEĞTĪLVEJĀNTVTGNRTVTGNRNDTNIK
OMOEDIISLĀNDOSLKESĪVETĀLGĀTĪLVEJĀNATVNYN-----NĀS---
                       (97)
         SF162
                     (101)
      TV1.8_2
      TV1.8_5
 TV2.12-5/1
                               QMHEDIISLWDQSLKPCVKLTPLCVTLNCTNTNVTGNRTVTGNSNSN A
   Consensus
                                                                                                             *200
                      (139) WKEMDRGEIKNCSKKVVIISIRNKMOKEYAJFYKTDVVEIDN----DNTSK
          SF162
                      (151) TGIYNIEEMKNCSFNATTELROKKHKRYELFYRIDINGLU--ENSDNFTY
      TV1.8_2
                      (151) NATYKYEEMKÜĞERNATTELEDEKHERYELEKTÜLVELN--ENSNNFTY
(141) -----KOMKÜĞERYETTELEDEKKERNETEKTÜLVELNIRKNGNINNY
      TV1.8 5
  TV2.12-5/1
                                 A Y EEMKNCSFNVTTELRDKKHKEYALFYKLDIVPLNN ENSNNFTY
   Consensus
                                                                                                                250
                      (185) KLINCNISVITOAGPKISFERI PLEVOAPAGEĀLIKCŅDKKENGSGEGITN
(199) RITKONESTITOAGEKVSFDEITLEVĀTĀGYĀLIKCŅNKERNGTGECVŅ
(199) RITKONESTITOAGEKVSEDDIJĒTĀSĀBĀDVALIKCŅNĶITĀGTGĒCVŅ
(185) RITKONISATITOĀGEKVSEDDĪDĪTĀKCĀRĀGYĀPLĶCŅNĶKĒNGLIĀPEDŅ
          SF162
       TV1.8_2
       TV1.8_5
  TV2.12-5/1
                       (201) RLINCHTSTITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFNGTGPCYN
    Consensus
                                 VSEVOCTHGIREVVSTONIINGSLAREGOVIRSENFRONAKTITVOLKES
                                 VSTVOCTHEIKEVVSTODILNESLÆEGIITRSENLÆNTRATIVHLNES
VSTVOCTHEIKEVVSTODILNESLÆEGIITRSENLÆNTRATIVHLNES
VSTVOCTHEIKEVVSTODILNESLÆEGIITRSENLÆNTRATIVHLNES
                       (235)
           SF162
        TV1.8 2
                        (249)
        TV1.8 5
   TV2.12-5/1
                        (235)
                       (251) VSTVQCTHGIKPVVSTQLLLNGSLAEEGIIIRSENLTENTKTIIVHLNES
    Consensus
                       (285) VEINCTRENNITERKSETTIGEERATTATGETIGDIROMENTISCEKWINTIL
(299) VEINCTRENNITERKSVRIGEGORVATINITERINISCEKWINTIL
(299) VEINCTRENNITERKSVRIGEGORVATINITERINISTERINISTICKWINTIL
(285) IETKOTRECHNITERSVRIGEGORVATIONICOPROARCHISKNEWITIL
           SF162
        TV1.8_2
        TV1.8_5
   TV2.12-5/1
                        (301) VEINCTRPNNNTRKSVRIGPGQAFYATNDIIGNIRQAHCNISTDRWNKTL
     Consensus
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400
                      (335) KOŢVŢĸĹĎAOFGNKŢ-ĒVŖKOSSĠŢŪPĒĻĬVMĮSĒŅŒĠĔŖŦŖĸĊŊĠŢŎĻŖŊ
(349) QOVMKĊĻĠĔĦŖPŊKŒ-ŢOŖKPĦĠĠŢŊĹŖŢŢMŖŒŖŢŖĠŖŦŖŶĠŊŢĠŊĿŖŊ
(349) QOVMKŢĴĠĔĦŖPŊKŬ-ĨĸŖĔ₽ĦŖĠĠŢĹŖŢŢĦŖĠĸĊŖĠĸŖŖŶĠŊŢĠŊĬŖŊ
(335) QRVSOKŊĠĔĹĔ₽ŊSŦĠĬĸŖĸŖŊŶĠĠŖĹŖŢŦŢŖĠĸŶĠĠŶŖŖŶĠŊŢŢŊŖŖŶ
        SF162
     TV1.8_2
     TV1.8_5
TV2.12-5/1
                       (351) QQVMKKLQEHFPNKT IKFKPHAGGDLEITMHSFNCRGEFFYCNTSNLFN
 Consensus
                                                                                                   β20/β21
                      SF162
     TV1.8_2
     TV1.8_5
TV2.12-5/1
                       (401) STYHN
                                                   NGTYKYNGNSS PITLQCKIKQIIRMWQGVGQAMYAPPIAG
  Consensus
                       (427) QIRCSSNITGLILTRIGEKEISNI--TEIRREGGDMRDNIRSELYKYKY
(445) NITCRSNITGTLITRIGERFNTTNN--TETREFCESTMRINNRSELYKYKY
(445) NITCRSNITGILLTRIGERFNTTNN-TETREFCESTMRINNRSELYKYKY
(433) NITCRSNITGILLTRIGEDNNTET---ETREFCESTMRINNRSELYKYKY
         SF162
      TV1.8 2
      TV1.8_5
TV2.12-5/1
                       (451) NITCRSNITGILLTRDGGFNNTNT TETFRPGGGDMRDNWRSELYKYKV
  Consensus
                                   501
                       (475) VKÏEPLEVAPTKĀKERVVOREKKĀVTĻCEMKUGĒMGĀGSĪMĒĀKSLTĪŠĪ
(493) VEJKPĪĢJĀPTKĻKĒRVVOREKĶĀVGIĢĀVĀGĀJĀGSĪMĒJĀBIJĒJĪ
(495) VEJKPĪĢĪKĀRRĪVVORKKĀVGIGĀVRĪGĀJĀGĀJĀGĀJĀJĀJĀ
(480) VEJKEJĀPĪTĀĀKRĪVVĒREKRĀGGIGĀVĀJĀGĀGĀJĀGĀJĀSIJĒJĪ
         SF162
      TV1.8 2
      TV1.8 5
TV2.12-5/1
                        (501) VEIKPLGIAPTKAKRRVVQREKRAVGIGAVFLGFLGAAGSTMGAASITLT
  Consensus
                                  AONAGITTECH AOODENII PETENOONINI OITAMATKA OSAKATUTEK EO
AONAGITTECH AOODENII PETENOONINI ON CHARLES AOOTENII PETENII
AONAGITTECH AOODINI IITAMATKA COMMINI MATAMATKA ON MATAMATKA
AONAGITTECH AOODINI IITAMATKA OOTINI OITAMATKA OOTINI TARATKA
AOONAGITTECH AOODINI IITAMATKA OOTINI OITAMATKA OOTINI TARATKA
                        (525)
          SF162
      TV1.8_2
      TV1.8_5
                        (545)
 TV2.12-5/1
                        (530)
                                   VQARQLLSGIVQQQSNLLKAIEAQQHMLQLTVWGIKQLQARVLAIERYLK
  Consensus
                        (551)
                                   601
                        (575) DOOLIGINGCEGKITCETAN PWNASWENTSLDQINNINTHNEGERETON
(593) DOOLIGINGCEGRITCETTAN PWNASWEST SEKOLINDINTHNEGERETON
(595) DOOLIGINGCEGRITCETAN PWNASWEST SEKOLINDINTHNEGERETON (595)
          SF162
      TV1.8_2
      TV1.8_5
                        (580) DOOLEGINGCEGERITETTINILWINSENERRYOSDIWDNINGWOODRELSNY
 TV2.12-5/1
                        (601) DQQLLGIWGCSGKLICTTAVPWNSSWSNKSEADIWDNMTWMQWDREISNY
   Consensus
                                    651
                        (625) ENLITTITEESONOOKKUROKUROKUASININEDISKULUVIKI EMI
(643) TGLITYNILLEDSONOOKKURKOLILEIDKUNUSKURDESNUPRETKUTIMI
(645) TETTERKILEDSONOOKKURKOLILEIDKUNUKUKTELIKUU
(630) TNIITRILEDSOSOOKKURKOLILAINKUNUKUKTEITIVILUVIKEITIVI
          SF162
       TV1.8 5
 TV2.12-571
                         (651) TNTIYRLLEDSQNQQEKNEKDLLELDKWNNLWNWFDISNWLWYIKIFIMI
   Consensus
                                    701
                                   YGGETGLEEVETVILGIVEVEGETSEEFFOTRFPAPRGEDREGGEREGG
VGGETGTETTEAVIS INTERVEGETSEEFFOTLTESERGLERINGEREGG
VGGETGTRITEAVISTAMERROGTSEPTSFOTLTESERGLERINGEREGGEREEGG
VGGITGERETEAVISERAMERROGTSEPTSFOTLTENEREFERLGGEREEGG
                         (675)
          SF162
       TV1.8 2
                         (693)
       TV1.8 5
                         (695)
 TV2.12-5/1
                         (701) VGGLIGLRIIFAVLSIVNRVRQGYSPLSFQTLTPSPRGPDRLGGIEEEGG
   Consensus
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(725) ERDRDRSSPAVHGLDADINEDERSKULFSKHEVERDLEDE ARINGLIGR-
(743) EODRDRSIRD SEFTSTAMED DER STEEN FRANKLINGELIGR-
(745) EODRDRSIRD SEFTSTAMED DES SEFTSTAMED DE LIVER DE LA VERNE DE LA VERN
                  TV1.8_2
                  TV1.8 5
TV2.12-5/1
                                                                         (751) EQDRDRSIRLVSGFLSLAWDDLRSLCLFSYHRLRDFILIAVRAVELLGHS
      Consensus
                                                                                                             801
                                                                         SF162
                  TV1.8 2
                  TV1.8_5
TV2.12-5/1
                                                                           (801) SLRGLQRGWEILKYLGSLVQYWGLELKKSAISLLDTIAIAVAEGTDRIIE
      Consensus
                                                                          (818) VAÓRIGRAFLHIRREGGERRALL-
(843) LVÓRICRAILNIFRAGRAGERALL-
(845) LVÓRICRAILNIBREGRALL-
(830) FLÓNECRGIRNVERREGGERALLO-
                               SF162
                  TV1.8 2
                  TV1.8 5
 TV2.12-5/1
                                                                           (851) LVQRICRAILNIPRRIRQGFEAALL
       Consensus
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Figure 103 (SEQ ID NO:134) depicts the nucleotide sequence of a synthetic Nefencoding polynucleotide derived from 12-5_1_TV2_C.ZA. The sequence includes a mutation at position 125 which results in a non-functional gene product.

Figure 104 (SEQ ID NO:135) depicts the nucleotide sequence of a synthetic Nefencoding polynucleotide derived from 12-5_1_TV2_C.ZA. The synthetic polynucleotide includes a mutation that eliminates the myristoylation site of the Nef gene product.

Figure 105 depicts an alignment of Env polypeptides from various HIV isolates. The regions between the arrows indicate regions (of TV1 and TV2 clones) in the beta and/or bridging sheet region(s) that can be deleted and/or truncated. The "*" denotes N-linked glycosylation sites (of TV1 and TV2 clones), one or more of which can be modified (e.g., deleted and/or mutated).

DETAILED DESCRIPTION OF THE INVENTION

The practice of the present invention will employ, unless otherwise indicated, conventional methods of chemistry, biochemistry, molecular biology, immunology and pharmacology, within the skill of the art. Such techniques are explained fully in the literature. See, e.g., Remington's Pharmaceutical Sciences, 18th Edition (Easton, Pennsylvania: Mack Publishing Company, 1990); Methods In Enzymology (S. Colowick and N. Kaplan, eds., Academic Press, Inc.); and Handbook of Experimental Immunology, Vols. I-IV (D.M. Weir and C.C. Blackwell, eds., 1986, Blackwell Scientific Publications); Sambrook, et al., Molecular Cloning: A Laboratory Manual (2nd Edition, 1989); Short Protocols in Molecular Biology, 4th ed. (Ausubel et al. eds., 1999, John Wiley & Sons); Molecular Biology Techniques: An Intensive Laboratory Course, (Ream et al., eds., 1998, Academic Press); PCR (Introduction to Biotechniques Series), 2nd ed. (Newton & Graham eds., 1997, Springer Verlag).

All publications, patents and patent applications cited herein, whether *supra* or *infra*, are hereby incorporated by reference in their entirety.